IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Akiyama et al. :
Serial No. 10/531,069 : Group Art Unit 1626
Filed April 11, 2005 : Examiner SHTERENGARTS,SAMANTHA L.
For: Controlled release preparation

DECLARATION UNDER 37 CFR §1.132

Honorable Commissioner of Patent and Trademarks, Alexandria, VA

Sir,

I, Takashi Kurasawa, declare:

That I am a citizen of Japan residing at 3-1, Shimogamoyakou-cho, Sakyo-ku, Kyoto-shi, Kyoto 606-0837, Japan;

That I was born on June 18, 1962 in Shiojiri-shi, Nagano , JAPAN;

That I graduated from Hokkaido University, with a degree of Master of Agriculture in March 1988;

That I have been an employee of Takeda Pharmaceutical Company Limited (formerly Takeda Chemical Industries Limited) since 1988, and I am currently Research Head, Pharmaceutical Technology Research & Development Laboratories, CMC Center, Takeda Pharmaceutical Company Limited, Osaka, Japan;

That I am one of the co-inventors of the United States Patent Application Serial No. 10/531,069 filed on April 11, 2005 and am familiar with the subject matter thereof;

The following experiment has been carried out under my direction and/or supervision.

(The Experiment Example A)

Five male beagle dogs were used for the experiment. The dogs were overnight-fasted but had free access to water during the experimental period. A capsule obtained in Example 59 (equivalent to 30mg of Compound A) was administered orally together with 30mL of tap water to each dog. Venous blood samples were collected for the assay of Compound A at 1, 2, 4, 6, 7 and 8h after administration. The plasma drug levels were measured by using HPLC with ultraviolet detection at 285nm. Mean plasma levels of Compound A of five dogs at 1, 2, 4, 6, 7and 8h after administration are shown in Table A. A capsule obtained in Example 59 showed significant duration of plasma drug levels.

Table A Plasma Levels of Compound A after Oral Administration of Capsules to Beagle Dogs

Plasma drug level (ng/mL)	1h	2h	4h	6h	7h	8h
A capsule obtained in Example 59	440	544	813	194	104	51

(The Experiment Example B)

Dissolution tests of the granules obtained in Example 53 and Example 56 were performed with USP dissolution apparatus 2 (paddle). Granules L-S (granules obtained in Example 53) and Granules H (granules obtained in Example 56) were tested under the following conditions:

Dissolution medium: pH6.8, 50mM phosphate buffer, 500mL

Rotation of paddle: 75rpm

At predetermined time periods, an aliquot was withdrawn and the percentage of released Compound A was spectrophotometrically determined at 286nm. The results are shown in Figure 1.

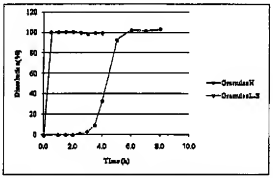

Figure 1. Release Profiles of Compound A from The Granules

It is declared by the undersigned that all statements made herein of his knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed this 4 th day of December 2009.

Takashi Kurasawa

Takashi KURASAWA